diastolic dimension (r=.65) and age (r=.81). There was no correlation between BNP and LVEF or JH/LVOT.
Conclusion: These data demonstrate elevated levels of BNP in patients with chronic AR and normal LV systolic function. Thus, even in patients who have no clinical evidence of cardiac decompensation, BNP levels may serve as a non-invasive marker of the valvular burden in a given patient, providing additional inexpensive and objective evidence of the severity of volume overload. These findings indicate that long-term prospective studies are warranted to determine the prognostic significance of BNP levels in patients with chronic AR.

1085-135 Pathological Fibrosis in Aortic Regurgitation Is Mediated by c-Jun/ATF-2 Complex Formation With cAMP Response Element in Cardiac Fibroblasts

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Background: We have shown that chronic aortic regurgitation (AR) causes myocardial fibrosis with excess matrix fibronectin (FN). Data suggest the SAPK/JNK pathway could modify FN gene expression by activating c-Jun/ATF-2 nuclear factors (nf) with complex formation between nf and the FN promoter. Methods: To test the role of this reaction in AR cardiac fibroblasts (CF), we assayed c-Jun/ATF-2 complex formation to FN cyclic AMP response element (FN-CRE) using electrophoretic mobility shifts in nuclear extracts of cultured CF from 5 nl NZW rabbits and 5 with chronic surgical AR (R fractions [F] =14%, 25%, 45%, 54%,>70%). Triplicate samples were prepared at passage 7. Nuclear extracts were incubated in DNA: protein binding buffer containing ^{32}P-labeled double-stranded FN-CRE oligonucleotides. Samples were separated by PAGE; gels were dried and exposed to X-ray film for videodensitometry. Specific binding of c-Jun/ATF-2 to FN-CRE was verified by competition assays with non-radioactive FN-CRE and by cJun/ATF-2 antibody supershifts. Results: Increased complex formation to FN-CRE was seen in 5/5 AR-CF lines (p=.03; See Table).
CRE complex formation correlated with AR severity (r^2=.26; p=.05). Conclusion: Chronic AR stimulates binding of c-Jun/ATF-2 to FN-CRE. Thus, increased FN expression by AR-CF may be mediated by increased c-Jun/ATF-2 complex formation to its promoter, activating transcription.

Cell Pair	%RF of AR	Rel. c-Jun/ATF-2-FN-CRE Complex Increase (AR:nl)
nl1 vs AR1	14	1.1:1.0
nl2 vs AR2	25	2.0:1.0
nl3 vs AR3	45	1.3:1.0
nl4 vs AR4	54	1.2:1.0
nl5 vs AR5	>70	3.0:1.0

1085-136 Impact of Vasodilator Use on Adverse Events in Chronic Severe Aortic Regurgitation

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Background: Vasodilating drugs (VDD) often are prescribed for *asymptomatic* pts with severe aortic regurgitation (AR) but impact of VDD on clinical outcomes in AR is unknown. Methods: To obtain this information we followed 83 consecutive *asymptomatic* unoperated pts with chronic severe AR and initially nl LV ejection fraction (EF) at rest (r) for 7±4 endpoint-free yrs. Pts were 81% male; age at study entry was 44±15 yrs. We used survival analysis to relate chronic use of VDD at study entry (ACE inhibitors: 8 pts [9.6%]; other VDD: in 3 pts [3.6%]) to survival (all cause death) and to cardiac event-free survival (events=cardiac death, subnl $LVEF_r$ or congestive symptoms). Drugs were prescribed prophylactically by primary physicians, not per protocol or based on clinical decline. Univariate comparisons of Kaplan-Meyer survival curves and Cox model analyses were performed sequentially to evaluate the potential confounding influence of baseline radionuclide cineangiographic $LVEF_r$, LVEF at peak exercise (ex) or change from r to ex, echocardiographic LV dimensions at diastole and systole, r and ex heart rates and blood pressures, gender, age, or chronic use of other cardiac drugs at study entry or during follow-up. Results: During follow-up, 5/83 pts (6.0%) died, 14 (16.9%) developed symptoms without subnl LVEF, and 9 (10.8%) developed subnl LVEF ± symptoms. Average annual risk of death was more than 4-fold greater among pts who had chronically used VDD (3.45%) than among those who had not (0.79%, p=.005). Average annual risk of cardiac events similarly was higher among pts who had chronically used VDD (13.79%) than among those who had not used VDD (average annual risk=3.75%, p=.01). No other variable confounded the observed association between VDD use and cardiac events (p=NS, all other variables). Conclusion: These findings suggest that chronic use of VDD may increase risk for cardiac events among *asymptomatic* pts with chronic severe AR and initially nl $LVEF_r$. Randomized clinical trials should be conducted to evaluate this association and, with it, the appropriateness of the widespread prophylactic use of VDD in AR.

POSTER SESSION

1109 Quantitation of Valve Disease

Monday, March 18, 2002, Noon-2:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1109-131 The Effect of Orifice Shape on the Normalized Velocity Distribution Method for the Quantification of Mitral Regurgitant Orifice Area

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Background: Recently, we proposed the normalized velocity distribution (NVD) method for the quantification of mitral valve regurgitation. Using computational fluid dynamics simulations, a relationship between the NVD along the centerline of the proximal convergence zone and normalized distance from the orifice was obtained. The regurgitant orifice area (ROA) can be estimated by non-linear least square fitting using the NVD-model: $v/v_p = 0.6 / (1+6.6*(r/\mathrm{sqrt}(ROA))^{1.8})$ where v is velocity from color M-mode (CMM), v_p is the peak velocity from continuous wave (CW) Doppler and r is the location along the centerline.
Initial in-vitro validation with circular orifices showed very promising results. Therefore, the purpose of this study was to investigate the effect of orifice shape on the performance of this new model.
Methods: CMM and CW Doppler images were obtained in an in-vitro model with various shaped orifices (width (w) by height (h) ratio from 1:1 to 1:10). Customized Labview code was developed to perform the nonlinear fitting of the Doppler data to the NVD model. Estimates of regurgitant orifice area were obtained and compared to the measured area to investigate the effect of the orifice shape.
Results: ROA estimates for circular orifices (ratio 1:1, reference standard) were in close agreement with the measured area ($y = 1.01x + 0.0003$, $r = 0.96$, $SE = 0.05cm^2$). Compared to the reference standard, an increase in the overestimation is observed with increasing ratio w/h. A linear correlation was found between the ratio w/h (x) and the percentage of error (y) in the estimation of ROA ($y = 10.6x - 14.2$, $r = 0.97$).
Conclusion: If the regurgitant orifice is circular, the ROA can be estimated with high accuracy using this method. However, an increasing error is made as the orifice becomes more elliptical in shape.

1109-132 A Semiautomatic Inter-Aliasing Distance Method for Quantifying Aortic Regurgitation Using Digital Color Doppler M-Mode Computation: In Vivo Study in a Chronic Animal Model

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Background: The accuracy of quantifying aortic regurgitation using flow convergence or vena contracta methods is limited by the ambiguity in identifying orifice center and the low temporal resolution of color Doppler. We developed a semiautomated method that is based on the inter-aliasing distance from color M-mode imaging to overcome these limitations and improve the reproducibility and accuracy by reducing user operation. **Methods:** The aortic valve was partially resected in 6 sheep prior to the study. Nineteen hemodynamic states (blood, nitoprusside and angiotensin administration) were studied in open chest sheep. Digital color M-mode data were obtained epicardially with a multiplane TEE probe and compared with aortic and pulmonary electromagnetic (EM) flow meters. On an off-line workstation, a set of adjustable curved borders was positioned on the aliasing lines to derive the instant regurgitant volume and flow rate. The velocities at the aliasing lines and the inter-aliasing distances were identified automatically from the digital data set without the need for the user to identify the orifice center using the algorithm employed in our custom program. **Results:** There was excellent correlation between regurgitant flow volume calculated by the M-mode method and EM results ($r=0.97$, $y=1.03x - 0.87$, $p<0.001$), there was also good correlation for peak flow rate ($r= 0.92$, $P<0.001$). **Conclusions:** This new color Doppler M-mode technique is reliable and reproducible for quantifying regurgitant flow.